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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,803	12/14/2005	Daniel T. Green	022354-000310US	7164

20350 7590 12/26/2006

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EXAMINER	
AUDET, MAURY A	
ART UNIT	PAPER NUMBER
1654	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/26/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,803	GREEN ET AL.	
	Examiner	Art Unit	
	Maury Audet	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,6,8-10,12 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,6,8-10,12 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response of 09/18/2006 is acknowledged. Claims 5-6, 8-10, 12-13 and new claims 18-25 are now pending, as drawn to products and methods of the combinational use of insulin and glucagon in e.g. diabetic control. The aim of using glucagon with standard insulin diabetic therapy, is premised on counteracting the hypoglycemic states inherent in standard insulin therapy.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5-6, 8-10, 12-13, and 18-25 (following amendment and the addition of new claims 18-25) are rejected under 35 U.S.C. 103(a) as being unpatentable over Houben et al. (US 6,572,542) in view of Trading et al. (Europ. J. of Pharm., 7 (1969), 206-10) and Unger et al. (US 5,542,935) (all previously cited).

Applicant's arguments have been considered but are not found persuasive. In summary, Applicant has argued, through individual separation of the references (argued persuasive as to the previous 102, anticipation rejection) that each is directed to a different invention related to the diabetic/hypoglycemic disease state and thus does not render obvious the present invention. Thereafter, Applicant's arguments may be summarized as: (the references are) lacking suggestion or motivation to combine, in order to arrive at the present invention. Were the

diabetic/hypoglycemic disease a new disorder, with little or no basis within its literature review or little ordinary skill in the art, this argument may carry more weight. However, such is not the case with this age old disease (diabetes/hypoglycemia), and under the analysis of one of *ordinary* skill in the art, based on *the combination* of these references *and* the knowledge carried by one of ordinary skill in the art at to this disease/disorder state, the references are deemed to still render obvious the presently amended method of use.

As previously discussed, Houben et al. teach an infusion pump comprising insulin and glucagons, in a formulation, in amounts therapeutically effective for the control of diabetes and treatment (and some degree of prevention, though not 100%) of hypoglycemia in a human or other mammal, wherein the steps are intrinsically within one minute to twelve hours of each other depending on the patients insulin/hypoglycemic state as monitored by the system, intrinsically separately administered depending on the patients need for insulin or glucagons in response to the glycemic state; in a diabetic patient who treated prior to suffering from hypoglycemic symptoms based on controls for response prior to; wherein the formulation is an infusion pump; for parenteral administration of insulin and/or glucagons; transdermally; comprising both insulin and glucagons; in a pump that controls administration of the respective drugs (entire document, especially e.g. claims 55-82; abstract; Figures 1-3; col. 2, lines 51-68).

Although Houben et al. generally contemplates any glucagons for infusion pump delivery, Houben et al. does not expressly recite "longer duration of action" glucagons (Applicant's claim 10). Additionally, although Houben et al. leaves open the containment of said glucagons in the infusion pump/formulations therein, Houben et al. does not expressly recite

that if be in a liposomal and/or microsphere formulation (Applicant's claims 12-13). [And it is noted (based on amendment and since not addressed in the previous action) that Houben et al. does not expressly teach the specific amounts of administration, such as "replacement dose of glucagon to a patient" or new ng/kg/min.].

Trading et al. teach the effectiveness of long acting (prolonged) glucagons for e.g. drug-induced (i.e. insulin-induced) hypoglycemia (title, col. 2, page 206).

Unger et al. teach improved formulation encapsulations for therapeutic agents such a glucagon, using microsphere, liposomal, and/or liposomal microsphere (col. 5, line 60; Fig. 8; col. 24, line 53).

As substantially previously recited, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to practice a method of reducing the risk of insulin-induced hypoglycemia, using any glucagon, including long duration or amount (e.g. basal glucagons amount or ng/kg/min.), using a combination of insulin and glucagon in Houben et al., because Houben et al. advantageously teach the use of an insulin/glucagon infusion pumps for treating hypoglycemia in Houben et al., because Trading et al. advantageously teach the effectiveness of long acting (prolonged) glucagons for e.g. drug-induced (i.e. insulin-induced) hypoglycemia, and one or ordinary skill in the art would have been motivated to use a combination approach to balance this well-known disease of diabetes, wherein both insulin and glucagons levels must be maintained in balance; including any patient specific amounts, by any route, which doctors or pharmacists are charged with routinely optimizing for the patient in question, absent evidence to the contrary.

As previously discussed, it would have also been obvious to one of ordinary skill in the art at the time the claimed invention was made to use any means of containing a formulation (e.g. liposomes, microspheres) comprising glucagons, including long duration glucagon, in the insulin/glucagons formulations for treating insulin-induced hypoglycemia in Houben et al., because Unger et al. advantageously teach improved formulation encapsulations for therapeutic agents such a glucagon, using microsphere, liposomal, and/or liposomal microsphere, and one or ordinary skill in the art would have been motivated to use an improved means of formulation for containing any glucagon used in the infusion pump therapy of Houben et al.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Citation of Pertinent Art (Repeated)

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Bremer et al. (Ch. 9, cited in Protein Delivery-Physical Systems, 1997, Plenum Press, pages 248-9; cited in Applicant's IDS of 03/20/2006) teaches an infusion pump of insulin and glucagons, with 6 minute phase displacement, for the control of glucose levels. However, the study was only conducted on "normal humans", and did not expressly teach the pump in the treatment of diabetes or in a diabetic patient.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 12/9/2006

Cecilia J. Tsang
Supervisory Patent Examiner
Technology Center 1600